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[Continued on next page]

(54) Title: PHARMACEUTICAL DOSAGE FORM BEARING PREGNANCY-FRIENDLY INDICIA

forms intended to be used during pregnancy from others.

(57) Abstract: A pharmaceutical dosage form comprising at least one active ingredient and destined for administration to pregnant women. The pharmaceutical dosage form bears pregnancy-friendly indicia apt to improve patient compliance with medically recommended dosage regimen resulting in improved product effectiveness. The pregnancy-friendly indicia is also apt toy diminish the incidence of erroneous dispensing of or erroneous ingestion of pharmaceutical dosage forms not intended for pregnant women. Also disclosed is a method for achieving improved patient compliance resulting in improved product effectiveness. Also disclosed is a method for diminishing the incidence of erroneous dispensing of or erroneous ingestion of dosage forms not intended for pregnant women. Said methods comprising providing a pharmaceutical dosage form, intended for use by pregnant women, bearing pregnancy-friendly indicia apt to graphically distinguish dosage

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Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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TITLE OF THE INVENTION

Pharmaceutical dosage form bearing pregnancy-friendly indicia

FIELD OF THE INVENTION

[0001] The present invention relates to pharmaceutical dosage forms intended for use during pregnancy.

BACKGROUND OF THE INVENTION

[0002] During pregnancy a variety of medical conditions require treatment with therapeutic agents. For instance, in Canada, excessive nausea and vomiting, possibly leading to hyperemesis gravidarum, are routinely treated with the prescription drug Diclectin® which contains a mixture in equal amounts of two active ingredients, namely pyridoxine HCl and doxylamine succinate.

[0003] Other conditions, pre-existing or developed during pregnancy, for example: diabetes, hypertension, blood cloths, depressive illness and heart disease are also commonly treated with prescription drugs.

[0004] In the case of pre-existing medical conditions numerous studies have shown that women have a tendency to abruptly stop taking their medications upon learning of the pregnancy, due to the perceived fear of birth defects[1]. In many cases, the risk to the health of the expectant mother and her baby is much higher if she stops or reduces her treatment than if she keeps taking the required medications.

[0005] Because of this perceived risk of harm to the fetus, otherwise known as the teratogenic risk, it is common for expectant mothers to discontinue taking a prescribed drug or to voluntarily diminish the prescribed dosage regimen. This often leads to dosage levels below therapeutic ranges in turn leading patients and

the medical community to incorrectly conclude that a particular drug is clinically ineffective.

[0006] Discontinuing or altering drug therapy, often against competent medical prescription, may have grave consequences indeed. The health of the expectant mother and vicariously of the fetus may be put at great risk because of poor compliance with competent medical prescription. In many instances, the teratogenic risks must be weighed against the risk of catastrophic illness or worsening condition on the part of the expectant mother.

[0007] Even discounting the particular problem of patient compliance during pregnancy, drug therapy patient compliance is a widespread and difficult problem in the medical community. Non-compliance with prescribed drug dosage regimen is a huge health problem for patients in general. For example, it is estimated that less than 25% of outpatients will complete a 10 day course of antibiotic therapy for a strep throat or otitis media.

[0008] Matsui[2] described that non-compliance with prescribed medication regimens may take many forms, including failure to fill the prescription, incorrect dosage, improper dosing interval, and premature discontinuation of the drug. Of course, the problem of non-compliance is magnified during pregnancy due to the importance of fetal safety.[3]

[0009] Whenever women delay or discontinue use of medications during pregnancy due to fears related to fetal safety, the result may be a worsening of the condition and hospitalisation with use of multiple drug therapy. Furthermore, depending of the underlying condition, the worsening of the condition has serious consequences even including suicidal ideation. Einarson showed in her study[1] on abrupt discontinuation of psychotropic drugs during pregnancy due to teratogenic fears, that 70.3% of women reported physical and psychological adverse effects to

the point that 29.7% reported suicidal ideation (one third of them were hospitalised).

[0010] Despite these appalling statistics, the perception of the expectant mother remains shrouded by well-known errors of the past such as the widely publicized cases of thalidomide-induced fetal malformations. The graphic evidence of birth defects attributed to Thalidomide exposure during early pregnancy has left a teratogenicity stigma on all medications. Hence, it is commonly thought that all medications are to be avoided during pregnancy. In the study entitled "*Prevention of Unnecessary Pregnancy Terminations by Counselling Women of Drug, Chemical, and Radiation Exposure During the First Trimester*", (1990)[4], Koren showed that pregnant women exposed to drugs that are known to be non teratogenic, still perceive that their born-to-be baby has a 24 % chance to suffer a major birth defect. This is about the same risk as an intra-uterine exposure to Thalidomide.

[0011] Scientific studies aimed at measuring the risk of drugs during pregnancy and patient education and counseling have so far been at the forefront of efforts to achieve better patient compliance with medical prescription.

[0012] However, even in the case of drugs having an extensively demonstrated record of fetal innocuousness, such as Diclectin® used to curb nausea and vomiting, the perception of latent risk remains. This perception of risk is of course carried over from the negative experiences of thalidomide which was also prescribed for nausea and vomiting during pregnancy and which was also provided as an oral dosage form. However, in reality, the active ingredient thalidomide and the active ingredients of Diclectin®, namely pyridoxine HCl and doxylamine succinate are completely unrelated. The risk perception carried-over from thalidomide is made apparent from patient compliance inquiries. Patient compliance with a medically prescribed dosage regimen of Diclectin® is clearly below what is recommend in the medical profession.

[0013] Even physicians and pharmacists are anxious about their liability associated with prescription or dispensing of medications to pregnant women. In the study by Pole[5], it was shown that even health care professionals, after reading four different labels (all of them stating that drug is safe to be used in pregnancy), have evaluated these labels, as bearing a residual risk. They were unable to fully perceive or accept that medication is safe to be used in pregnancy. Patients, physicians and pharmacists are also worried about erroneous ingestion or dispensing of drugs not intended for use during pregnancy.

[0014] Despite the enormous volume of scientific evidence supporting Diclectin® harmlessness to the fetus, pregnant women persistently do not follow their physician's recommendation as to the adherence to Diclectin® dosage regimen. In most cases, women voluntarily reduce the dosage by half. In fact, they do not comply with the proper dosage regimen for Diclectin® to the point that some woman and some physicians believe that the medication is not effective. Therefore, non-compliance often results in a perception of product effectiveness failure.

[0015] Due to non-compliance with medical prescription, patients using less than prescribed amounts of Diclectin® will often find themselves in sub-therapeutic state. This prevents the medication from being effective and may aggravate the mother's condition to the point of developing hyperemesis gravidarum (HG). HG is the most severe end of nausea and vomiting during pregnancy, when a pregnant woman suffers from loss of more than 5% of her pre-pregnancy body weight, dehydration, acid-base disturbances, ketonuria and electrolyte imbalance. At this stage, physicians use intravenous medications that are often not recognised for safe use during pregnancy in order to control maternal condition. The use of these medications poses an unnecessary risk to the fetus. If this last resort medication appears to be ineffective due to the deterioration of the woman's condition, a therapeutic abortion may even be considered[6].

[0016] In order to diminish potential for birth defects a vitamin intake is now medically recommended during pregnancy. For example, clinical evidence shows that taking folic acid before conception and during the first trimester of pregnancy may prevent up to 72% of the congenital abnormalities spina bifida and anencephaly[7]. Despite this, pregnant women are generally non compliant with recommended folic acid intake treatment thus putting an unborn child at an increased risk of major birth defect.

[0017] The situation is even worse if pregnant woman has been on a drug therapy that interferes with folic acid receptors (e.g., phenobarbital, phenytoin, carbamazepine, valproic acid). In this case, a pregnant woman is even at greater risk for having a baby with birth defect if she is not compliant.

[0018] Thus there remains an important need for innovative solutions to achieve better patient compliance of vitamins or drugs recommended for use during pregnancy.

OBJECTS OF THE INVENTION

[0019] An object of the present invention is therefore to provide an improved oral dosage form for, *inter alia*, achieving better patient compliance with vitamins or drugs intended for use during pregnancy.

[0020] Another object is to provide a method for improving patient compliance of pregnant women by diminishing their perception of teratogenic risk and by direct implication to improve product effectiveness of dosage forms containing at least one active ingredient and intended for use by pregnant women.

[0021] A further object is to provide a method for diminishing the incidence of erroneous ingestion by pregnant women or of erroneous dispensing by pharmacists of therapeutic agents not prescribed to said pregnant women.

SUMMARY OF THE INVENTION

[0022] More specifically, in accordance with the present invention, there is provided a pharmaceutical dosage form comprising at least one active ingredient, such as for example a vitamin supplement or a synergistic combination of pyridoxine HCl and doxylamine succinate, and destined for administration to pregnant women, the pharmaceutical dosage form bearing pregnancy-friendly indicia. In a preferred embodiment the pregnancy-friendly indicia is in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging. In a most preferred embodiment, the dosage form is destined for oral administration.

[0023] Also provided is a method of diminishing the perception of teratogenic risk among pregnant women taking a pharmaceutical dosage form containing at least one active ingredient. The method comprising providing said pharmaceutical dosage form bearing pregnancy-friendly indicia, preferably in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

[0024] Also provided is a method of improving patient compliance of pregnant women with medically recommended dosage regimen of at least one active ingredient. The method comprising providing a pharmaceutical dosage form bearing pregnancy-friendly indicia. Improving patient compliance also leads to improved product effectiveness because product effectiveness is linked to patient compliance. Thus, the method of the present invention also leads to improved product effectiveness.

[0025] Also provided is method of diminishing the incidence of erroneous ingestion by pregnant women or of erroneous dispensing by pharmacists of therapeutic agents not prescribed to said pregnant women. The method comprising providing a pharmaceutical dosage form comprising at least one active ingredient prescribed to said pregnant women, the dosage form bearing

pregnancy-friendly indicia apt to graphically distinguish dosage forms intended to be used during pregnancy from others.

[0026] Other objects, advantages and features of the present invention will become more apparent upon reading of the following non-restrictive description of preferred embodiments thereof, given by way of example only with reference to the accompanying drawing.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] Figure 1 is a pictorial representation of an improved oral dosage form in accordance with the present invention and bearing a visible indicia apt to achieve improved patient compliance.

DESCRIPTION OF THE PREFERRED EMBODIMENT

[0028] The main object of the present invention is therefore to provide an improved oral dosage form for achieving better patient compliance with drugs prescribed for use during pregnancy. This objective is surprisingly and effectively achieved by applying pregnancy-friendly indicia on the dosage form. Dosage form is understood to encompass its packaging. By "pregnancy-friendly" indicia is meant any graphical or textual representation apt to be easily recognized as indicative of a safe medication for taking during pregnancy.

[0029] In a most preferred embodiment, the pregnancy-friendly indicia are a graphical representation of the profile of a pregnant woman having a hand resting on her stomach region. Such graphical representation is illustrated in Figure 1 and has a particularly comforting effect on expectant mothers and have been statistically shown to substantially lower the perception of teratogenic risk and consequently lead to elevated patient compliance. Such evidence is presented in the examples provided below.

Example 1

[0030] A study was conducted with 12 pregnant women. This study was aimed at testing if pregnancy-friendly indicia such as the indicia illustrated in Figure 1 may have a positive impact by reducing the perception of teratogenic risk of a drug taken during pregnancy, and if it is the case, which kind of design is most effective in improving patient compliance.

[0031] Different designs of pregnancy-friendly indicia were printed on tablets. This aim was to ascertain if, when used, those indicia would increase the patients' confidence in taking the tablet during pregnancy by reducing the perception of teratogenic risk. Diminishing the perception of teratogenic risk would consequently improve patient compliance and as a result achieve better treatment effectiveness.

[0032] The study revealed while all pregnancy-friendly indicia are helpful at diminishing the perception of teratogenic risk, the most preferred graphical representation is that of Figure 1. The graphical representation shown in Figure 1 would indicate in a clear and precise fashion that the medication has been specifically designed for the pregnant woman.

[0033] This surprising positive effect on patient compliance would of course translate itself in the effectiveness of a vitamin or drug treatment and a concurrent reduction of medical complications for the pregnant woman and the fetus.

Example 2

[0034] To further validate the findings disclosed in Example 1, an observational, prospective survey on pregnant women in family practice offices and obstetrician offices was conducted. The statistical tool used for measuring the objective of the study (how reassured about fetal safety woman feels taking one or the other tablet once prescribed to them) was a validated scientific tool for

subjective measurements: a visual analog scale (VAS) from 1-5 (1 being the least safe and 5 being the most safe). Patients were told that the prescribed drug, in tablet form, was safe for use in pregnancy and were asked to label on the VAS how reassured about fetal safety they felt when taking the tablet. They were shown two different tablets, one plain white and the other white with the illustration of Figure 1 applied to the tablet.

[0035] Data was collected from 132 pregnant women and the results are shown in the table below:

Test: Dual-Sample Assuming Equal Variances

Teratogenic Risk Perception on Scale of 1 to 5 with 1 being greatest risk perception.

	Plain White tablet	**Tablet with pregnancy-friendly indicia as per Figure 1**	
Observations	132	132	
Mean Risk Perception	2,5227	3,6969	
Variance	1,2132	1,3120	
P(T<=t) one-tail			P< 0.0001

[0036] The study clearly showed superiority of the tablet with a printed pregnant woman concerning the perception of the teratogenic risk (results were statistically significant with P<0.0001). The P value of 0.0001 signifies that the result of this study as 1/10,000 chance to be the result of chance only. If we repeat this study 10,000 times, in 9,999 cases, the same results would be obtained. Usually P<0.05 is recognized as medically significant.

[0037] Thus, in the sample group of 132 pregnant women, 23.4% felt more reassured about the fetal safety of taking the tablet with a printed pregnant woman as shown in Figure 1, than a plain white tablet.

[0038] Of course, these results would translate themselves directly into improved patient compliance by a margin of at least 23.4%. Thus, a strong conclusion emerges that the presence of pregnancy-friendly indicia on a vitamin or drug to be taken during pregnancy will significantly reduce teratogenic risk perception and by the same token improve patient compliance with prescribed dosage regimen.

[0039] Although the present invention has been described hereinabove by way of preferred embodiments thereof, it can be modified, without departing from the spirit and nature of the subject invention as defined in the appended claims. More specifically, the exact appearance of pregnancy-friendly indicia is variable with the understanding that some indicia will induce greater patient compliance than others. Also, it is to be understood that although examples were given in relation to oral tablets, other pharmaceutical dosages forms are of course covered by the present invention. Thus, pregnancy-friendly indicia may appear on the actual dosage form, such as tablet, sugar coated tablet, sublingual tablet, caplet, capsule, gel capsule, chewable tab, pill, suppository, powder, vial, ampoule, pre-filled syringe, nasal spray, pastille, syrup, drops, vaginal ovule, subcutaneous implant, transdermal gel, transdermal patch, transmucausal strip, pouch, or may also appear on the packaging and labeling of the dosage form.

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WHAT IS CLAIMED IS:

1. A pharmaceutical dosage form comprising at least one active ingredient and destined for administration to pregnant women, said pharmaceutical dosage form bearing pregnancy-friendly indicia adapted to graphically confirm the non-teratogenic aspect of the pharmaceutical dosage form.

2. The pharmaceutical dosage form of claim 1 wherein the dosage form is an oral dosage form.

3. The pharmaceutical dosage form of claim 2 wherein the dosage form is a tablet.

4. The pharmaceutical dosage form of claim 1 wherein the at least one active ingredient comprises at least one vitamin.

5. The pharmaceutical dosage form of claim 1 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

6. A pharmaceutical dosage form comprising at least one active ingredient and destined for administration to pregnant women, said pharmaceutical dosage form bearing pregnancy-friendly indicia adapted to graphically confirm the non-teratogenic aspect of the pharmaceutical dosage form, said indicia being in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

7. The pharmaceutical dosage form of claim 6 wherein the dosage form is a tablet and the graphical illustration is applied to the tablet surface.

8. The pharmaceutical dosage form of claim 6 wherein the at least one active ingredient comprises at least one vitamin.

9. The pharmaceutical dosage form of claim 6 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

10. A method of diminishing the perception of teratogenic risk among pregnant women taking a pharmaceutical dosage form containing at least one active ingredient, said method comprising providing pregnant women with the pharmaceutical dosage form bearing pregnancy-friendly indicia so as to graphically confirm the non-teratogenic aspect of the pharmaceutical dosage form.

11. The method of claim 10 wherein said pregnancy-friendly indicia is in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

12. The method of claim 10 wherein the at least one active ingredient comprises at least one vitamin.

13. The method of claim 10 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

14. The method of claim 10 wherein the pharmaceutical dosage form is an oral dosage form.

15. A method of improving patient compliance of pregnant women with medically recommended dosage regimen of at least one active ingredient, said method comprising providing pregnant women with a pharmaceutical dosage form bearing pregnancy-friendly indicia so as to graphically confirm the non-teratogenic aspect of the pharmaceutical dosage form and thereby achieve greater patient compliance with the medically recommended dosage regimen.

16. The method of claim 15 wherein said pregnancy-friendly indicia is in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

17. The method of claim 15 wherein the at least one active ingredient comprises at least one vitamin.

18. The method of claim 15 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

19. The method of claim 15 wherein the pharmaceutical dosage form is an oral dosage form.

20. A method of improving patient compliance of pregnant women with medically recommended dosage regimen of at least one active ingredient and consequently and simultaneously improving the therapeutic effectiveness of said active ingredient(s), said method comprising providing pregnant women with a pharmaceutical dosage form bearing pregnancy-friendly indicia to graphically confirm the non-teratogenic aspect of said dosage form so as to elicit better patient compliance with the medically recommended dosage regimen.

21. The method of claim 20 wherein said pregnancy-friendly indicia is in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

22. The method of claim 20 wherein the at least one active ingredient comprises at least one vitamin.

23. The method of claim 20 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

24. The method of claim 20 wherein the pharmaceutical dosage form is an oral dosage form.

25. A method of diminishing the incidence of erroneous ingestion by pregnant women of therapeutic agents not prescribed to said pregnant women, said method comprising providing pregnant women with a pharmaceutical dosage form comprising at least one active ingredient prescribed to said pregnant women, said dosage form bearing pregnancy-friendly indicia apt to graphically distinguish dosage forms intended to be used during pregnancy from others.

26. The method of claim 25 wherein said pregnancy-friendly indicia is in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

27. The method of claim 25 wherein the at least one active ingredient comprises at least one vitamin.

28. The method of claim 25 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

29. The method of claim 25 wherein the dosage form is an oral dosage form.

30. A method of diminishing the incidence of erroneous dispensing of pharmaceutical dosage forms not intended for pregnant women, said method comprising providing a pharmaceutical dosage form, intended for use by pregnant women, comprising at least one active ingredient and bearing pregnancy-friendly indicia apt to graphically distinguish dosage forms intended to be used during pregnancy from others.

31. The method of claim 30 wherein said pregnancy-friendly indicia is in the shape of a graphical illustration of a pregnant woman applied to the dosage form itself or to its packaging.

32. The method of claim 30 wherein the at least one active ingredient comprises at least one vitamin.

33. The method of claim 30 wherein the at least one active ingredient comprises the active ingredients pyridoxine HCl and doxylamine succinate.

34. The method of claim 30 wherein the dosage form is an oral dosage form.

FIG. 1

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 03/00977

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/20 A61K31/4415 A61K31/4402

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, EMBASE, WPI Data, PAJ, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 457 895 A (THOMPSON ANDREW R ET AL) 17 October 1995 (1995-10-17) column 1, line 38 - line 48	1-34
X	WO 97 48384 A (JANSSEN PHARMACEUTICA NV ;POSAGE GARY W (US)) 24 December 1997 (1997-12-24) page 7, line 32 claim 1	1-34
X	EP 1 149 572 A (SHINETSU CHEMICAL CO) 31 October 2001 (2001-10-31) page 5, line 57 - line 58 page 7, line 17 - line 26 example 7	1-34

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 September 2003	26/09/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hedegaard, A

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PEDERSEN M: "Tabtet tooling: Design, maintenance and troubleshooting" PHARMACEUTICAL TECHNOLOGY EUROPE 1999 UNITED KINGDOM, vol. 11, no. 2, 1999, pages 22-28, XP009016627 ISSN: 0164-6826 abstract	1-34
X	MUNO F J JR: "Broadening utility of tablet and capsule imprints" JOURNAL OF PHARMACY PRACTICE 2000 UNITED STATES, vol. 13, no. 2, 2000, pages 130-140, XP009017312 ISSN: 0897-1900 the whole document	1-34
A	US 6 340 695 B1 (GERVAIS ERIC) 22 January 2002 (2002-01-22) the whole document	1-34
A	BISHAI R ET AL: "The efficacy and safety of Diclectin(R) (doxylamine/pyridoxine) for nausea and vomiting of pregnancy" TODAY'S THERAPEUTIC TRENDS 1999 UNITED STATES, vol. 17, no. 2, 1999, pages 167-179, XP009016726 ISSN: 0741-2320 the whole document	1-34

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 03/00977

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: –
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(v) PCT – Presentation of information. Although claims 1-34 are directed to a presentation of information, the search has been carried out and based on the alleged effects of the dosage form.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/CA 03/00977

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